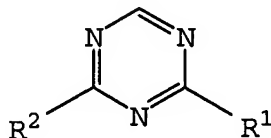


The listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

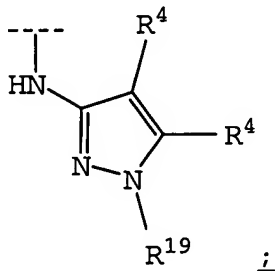
Claims 1-20 (Canceled).

Claim 21 (Currently amended) A compound having the formula: ~~The compound of claim 1~~



wherein,

~~Each R¹ is independently~~



wherein

R¹⁹ is independently H or C1-C6 alkyl;

R² is -NHR³, -NHR⁵, -NHR⁶, -NR⁵R⁵ or -NR⁵R⁶;

R³ is independently aryl, phenyl optionally substituted with 1-5 independent R⁴ on each ring, or heteroaryl optionally substituted with 1-4 independent R⁴ on each ring;

R⁴ is independently selected from H, C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, aryl, R⁸, halo, CF₃, SR⁵, OR⁵, OC(O)R⁵, NR⁵R⁵, NR⁵R⁶, NR⁵R¹⁶, COOR⁵, NO₂, CN, C(O)R⁵, C(O)C(O)R⁵, C(O)NR⁵R⁵, S(O)_nR⁵, S(O)_nNR⁵R⁵, NR⁵C(O)NR⁵R⁵, NR⁵C(O)C(O)R⁵, NR⁵C(O)R⁵, NR⁵(COOR⁵), NR⁵C(O)R⁸, NR⁵S(O)_nNR⁵R⁵, NR⁵S(O)_nR⁵, NR⁵S(O)_nR⁸, NR⁵C(O)C(O)NR⁵R⁵, NR⁵C(O)C(O)NR⁵R⁶, OC(O)NR⁵R⁵, OS(O)_nNR⁵R⁵, NR⁵S(O)_nOR⁵, P(O)(OR⁵)₂, C1-C10 alkyl substituted with 1-3 independent

aryl, R⁷ or R⁸, or
C2-C10 alkenyl substituted with 1-3 independent aryl, R⁷ or R⁸;
n is independently 1 or 2;
R⁵ is independently H, C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl,
C3-C10 cycloalkyl, C4-C10 cycloalkenyl, aryl, R⁹, haloalkyl,
C1-C10 alkyl substituted with 1-3 independent aryl, R⁷ or R⁹
groups,
C3-C10 cycloalkyl substituted with 1-3 independent aryl, R⁷ or
R⁹ groups, or
C2-C10 alkenyl substituted with 1-3 independent aryl, R⁷ or R⁹,
R⁶ is independently C(O)R⁵, COOR⁵, C(O)NR⁵R⁵, C(=NR⁵)NR⁵R⁵, or S(O)_n
R⁵;
R⁷ is independently halo, CF₃, SR¹⁰, OR¹⁰, OC(O)R¹⁰, NR¹⁰R¹⁰, NR¹⁰R¹¹,
NR¹¹R¹¹, COOR¹⁰, NO₂, CN, C(O)R¹⁰, OC(O)NR¹⁰R¹⁰, C(O)NR¹⁰R¹⁰,
N(R¹⁰)C(O)R¹⁰, N(R¹⁰) (COOR¹⁰), S(O)_nNR¹⁰R¹⁰, NR¹⁰S(O)_nNR¹⁰R¹⁰,
NR¹⁰S(O)_nR¹⁰ or P(O)(OR⁵)₂;
R⁸ is independently a 3-8 membered monocyclic, 7-12 membered
bicyclic, or 11-14 membered tricyclic ring system having 1-3
heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9
heteroatoms if tricyclic, said heteroatoms independently selected
from O, N, or S, which may be saturated or unsaturated, and
wherein 0, 1, 2, 3 or 4 atoms of each ring may be substituted by
a substituent independently selected from C1-C10 alkyl, C2-C10
alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10
cycloalkenyl, aryl, R⁹, halo, sulfur, oxygen, CF₃, SR⁵, OR⁵,
OC(O)R⁵, NR⁵R⁵, NR⁵R⁶, NR⁶R⁶, COOR⁵, NO₂, CN, C(O)R⁵, C(O)NR⁵R⁵,
S(O)_nNR⁵R⁵, NR⁵C(O)NR⁵R⁵, NR⁵C(O)R⁹, NR⁵S(O)_nNR⁵R⁵, NR⁵S(O)_nR⁹,
C1-C10 alkyl substituted with 1-3 independent R⁷, R⁹ or
aryl, or
C2-C10 alkenyl substituted with 1-3 independent R⁷, R⁹ or
aryl;
R⁹ is independently a 3-8 membered monocyclic, 7-12 membered
bicyclic, or 11-14 membered tricyclic ring system having 1-3
heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9
heteroatoms if tricyclic, said heteroatoms independently selected

from O, N, or S, which may be saturated or unsaturated, and
wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a
substituent independently selected from C1-C10 alkyl, C2-C10
alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl,
halo, sulfur, oxygen, CF₃, SR¹⁰, OR¹⁰, NR¹⁰R¹⁰, NR¹⁰R¹¹, NR¹¹R¹¹,
COOR¹⁰, NO₂, CN, C(O)R¹⁰, S(O)_nR¹⁰, S(O)_nNR¹⁰R¹⁰ or C(O)NR¹⁰R¹⁰;
R¹⁰ is independently H, C1-C10 alkyl, C2-C10 alkenyl, C2-C10
alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, haloalkyl,
C1-C10 alkyl optionally substituted with 1-3 independent
substituents selected from C1-C10 alkyl, C2-C10 alkenyl, C2-
C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo,
CF₃, OR¹², SR¹², NR¹²R¹², COOR¹², NO₂, CN, C(O)R¹², C(O)NR¹²R¹²,
NR¹²C(O)R¹², N(R¹²)(COOR¹²), S(O)_nNR¹²R¹² or OC(O)R¹², or
phenyl optionally substituted with 1-3 independent substituents
selected from C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl,
C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF₃, OR¹², SR¹²,
NR¹²R¹², COOR¹², NO₂, CN, C(O)R¹², C(O)NR¹²R¹², NR¹²C(O)R¹²,
N(R¹²)(COOR¹²), S(O)_nNR¹²R¹² or OC(O)R¹²;
R¹¹ is independently C(O)R¹⁰, COOR¹⁰, C(O)NR¹⁰R¹⁰ or S(O)_nR¹⁰;
R¹² is independently H, C1-C10 alkyl, C2-C10 alkenyl, C2-C10
alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl,
C1-C10 alkyl substituted with 1-3 independent substituents
selected from C2-C10 alkenyl, C2-C10 alkynyl, C3-C10
cycloalkyl, C4-C10 cycloalkenyl, halo, CF₃, OR¹³, SR¹³, NR¹³R¹³,
COOR¹³, NO₂, CN, C(O)R¹³, C(O)NR¹³R¹³, NR¹³C(O)R¹³ or OC(O)R¹³, or
phenyl optionally substituted with 1-3 independent substituents
selected from C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl,
C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF₃, OR¹³, SR¹³,
NR¹³R¹³, COOR¹³, NO₂, CN, C(O)R¹³, C(O)NR¹³R¹³, NR¹³C(O)R¹³ or
OC(O)R¹³;
R¹³ is independently H, C1-C10 alkyl, C2-C10 alkenyl, C2-C10
alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl,
C1-C10 alkyl optionally substituted with halo, CF₃, OR¹⁴, SR¹⁴,
NR¹⁴R¹⁴, COOR¹⁴, NO₂ or CN, or

phenyl optionally substituted with halo, CF₃, OR¹⁴, SR¹⁴, NR¹⁴R¹⁴,
 COOR¹⁴, NO₂ or CN;
R¹⁴ is independently H, C1-C10 alkyl, C3-C10 cycloalkyl or phenyl;
R¹⁶ is independently H, C1-C10 alkyl, C2-C10 alkenyl, C2-C10
 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, aryl, R⁸, halo,
 CF₃, COOR⁵, C(O)R⁵, C(O)C(O)R⁵, C(O)NR⁵R⁵, S(O)_nR⁵; S(O)_nNR⁵R⁵,
 C1-C10 alkyl substituted with 1-3 independent aryl, R⁷ or R⁸,
 or
 phenyl optionally substituted with substituted with 1-4
 independent R²³, or
 C2-C10 alkenyl substituted with 1-3 independent aryl, R⁷ or R⁸;
 and
 R²³ is independently selected from H, C1-C10 alkyl, C2-C10 alkenyl,
 C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, aryl, R⁸,
 halo, CF₃, SR⁵, OR⁵, OC(O)R⁵, NR⁵R⁵, NR⁵R⁶, COOR⁵, NO₂, CN, C(O)R⁵,
 C(O)C(O)R⁵, C(O)NR⁵R⁵, S(O)_nR⁵; S(O)_nNR⁵R⁵, NR⁵C(O)NR⁵R⁵,
 NR⁵C(O)C(O)R⁵, NR⁵C(O)R⁵, NR⁵(COOR⁵), NR⁵C(O)R⁸, NR⁵S(O)_nNR⁵R⁵,
 NR⁵S(O)_nR⁵, NR⁵S(O)_nR⁸, NR⁵C(O)C(O)NR⁵R⁵, NR⁵C(O)C(O)NR⁵R⁶,
 OC(O)NR⁵R⁵, OS(O)_nNR⁵R⁵, NR⁵S(O)_nOR⁵, P(O)(OR⁵)₂,
 C1-C10 alkyl substituted with 1-3 independent aryl, R⁷ or R⁸,
 or
 C2-C10 alkenyl substituted with 1-3 independent aryl, R⁷ or R⁸.

Claim 22 (Currently amended): A composition comprising a
 compound of any of claims 1-21 and 32 and a pharmaceutically
 acceptable carrier.

Claim 23 (Original): The composition of claim 22, further
 comprising at least one additional therapeutic agent.

Claims 24-26 (Canceled).

Claim 27 (Currently amended): A method of inhibiting
 angiogenesis or vasculogenesis activity in a mammal comprising

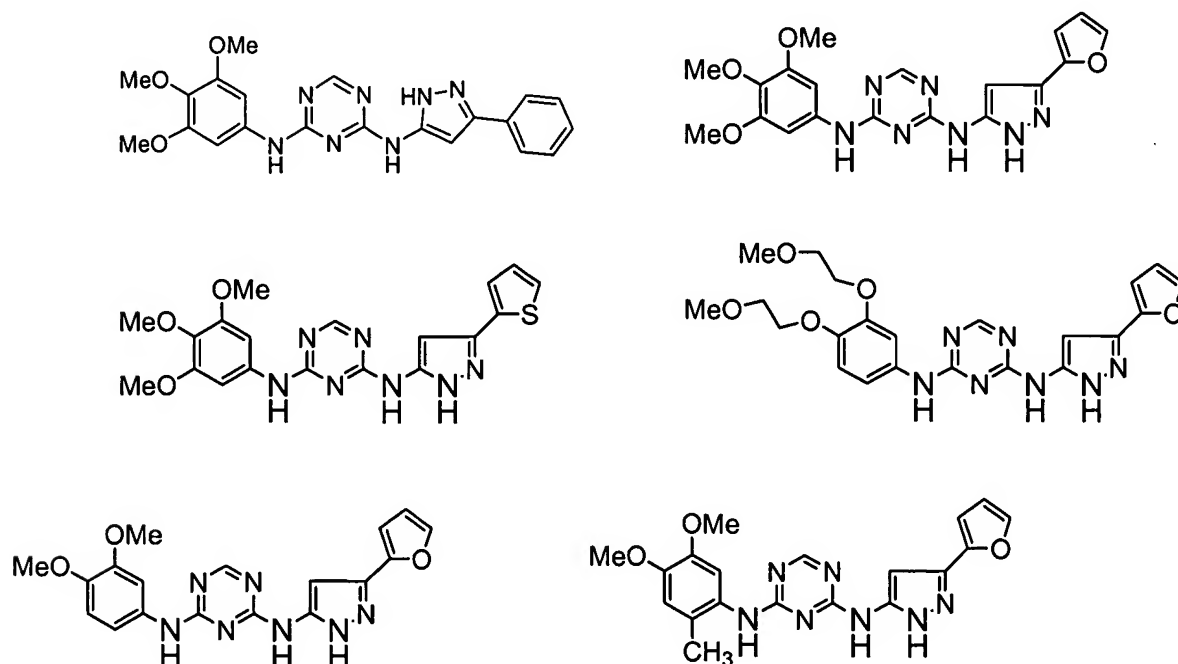
administration of a composition comprising an effective amount of a
compound of any of claims 1-21 and 32.

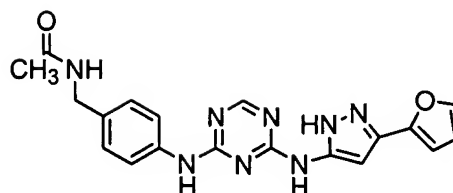
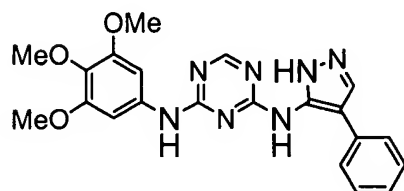
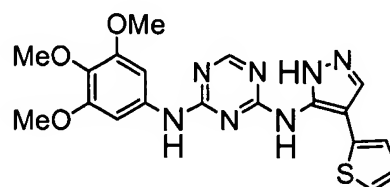
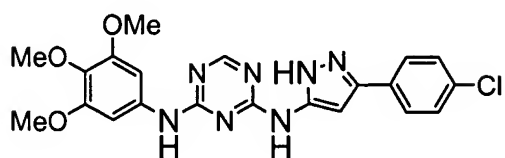
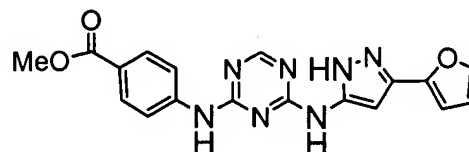
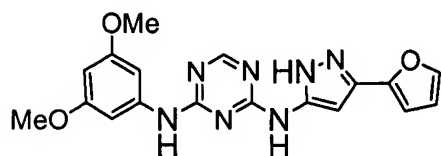
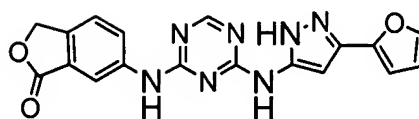
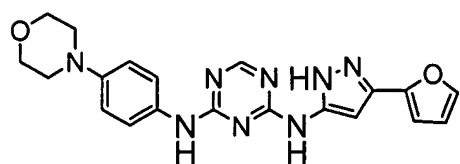
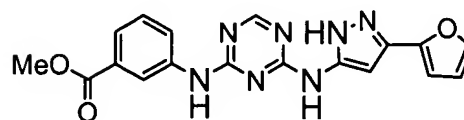
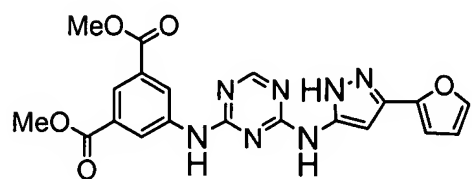
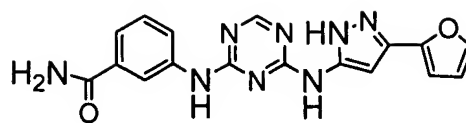
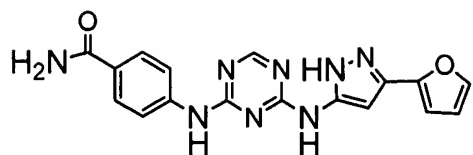
Claim 28 (Currently amended): A method of making a
pharmaceutically useful composition comprising combining an effective
amount of a compound of any of claims 1-21 and 32 with one or more
pharmaceutically acceptable carriers.

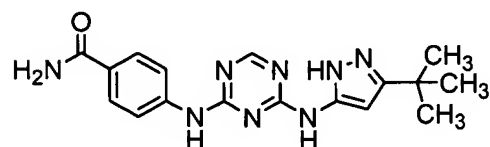
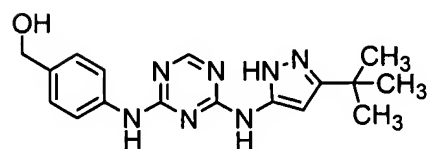
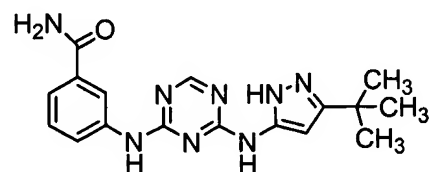
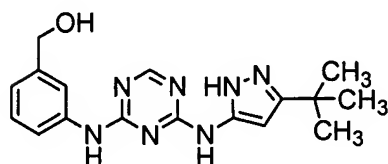
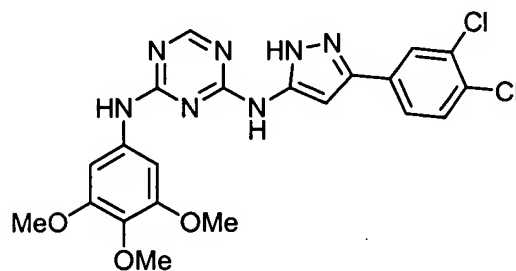
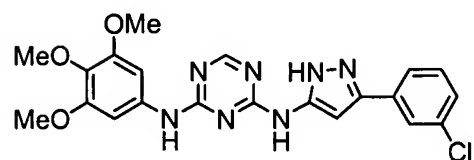
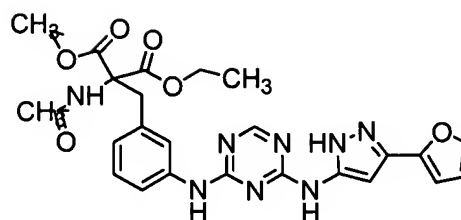
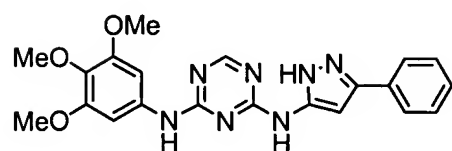
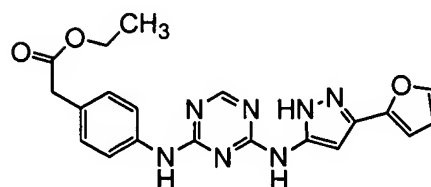
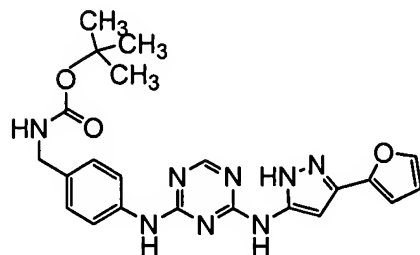
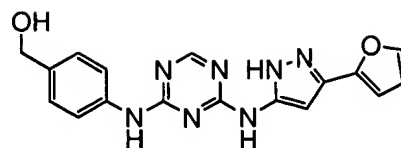
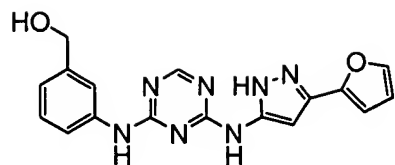
Claim 29 (Currently amended): The method of claim 28, further
comprising combining an effective amount of an additional therapeutic
agent.

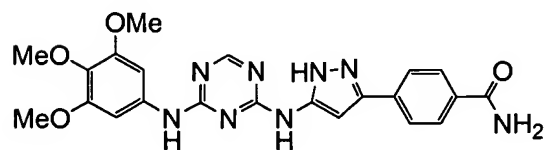
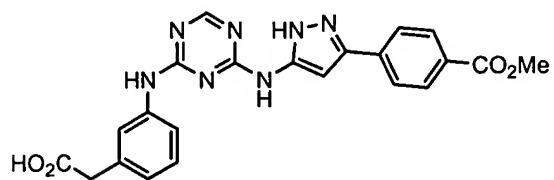
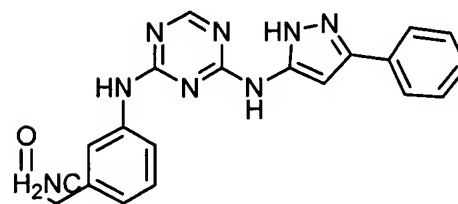
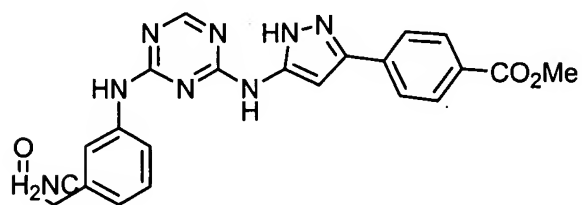
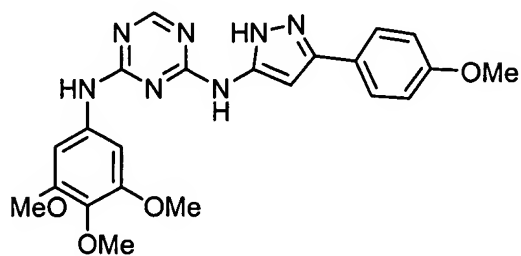
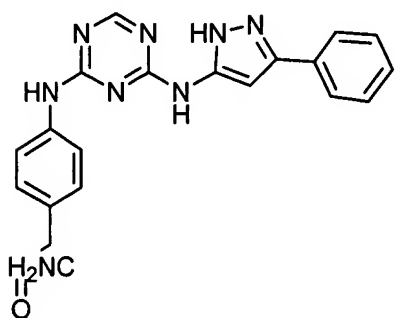
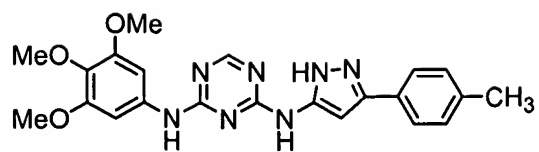
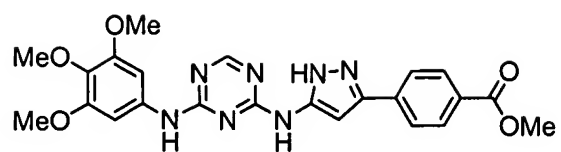
Claim 30-31 (Canceled).

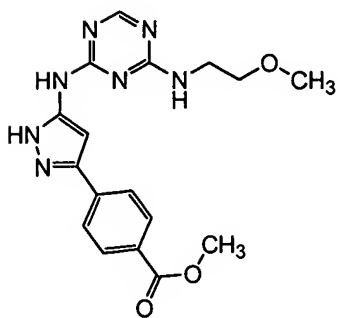
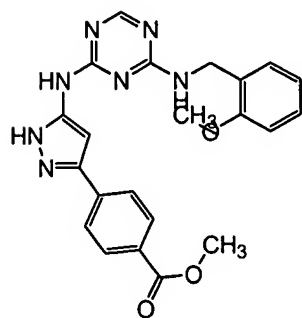
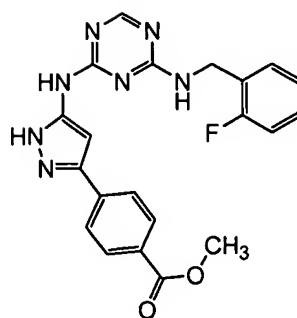
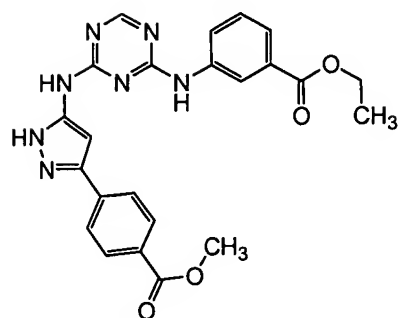
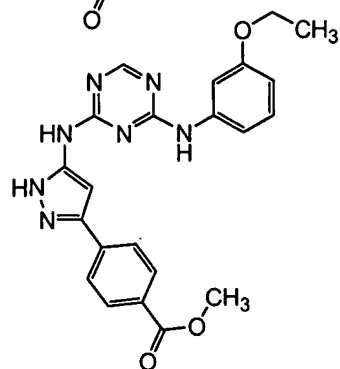
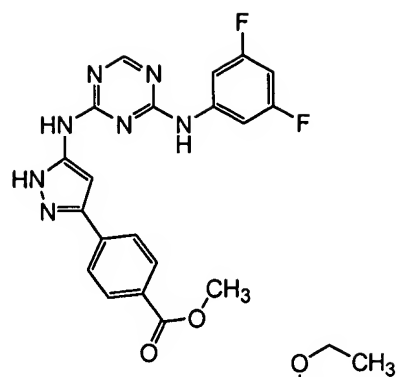
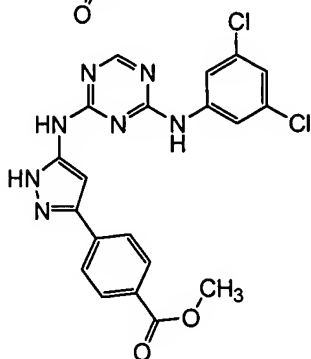
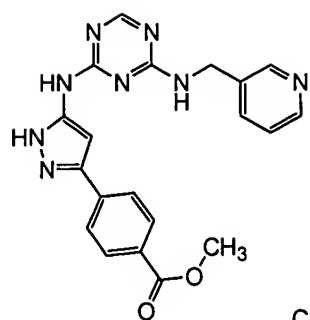
Claim 32 (New): Compound of Claim 22 and a pharmaceutically
acceptable salt thereof selected from

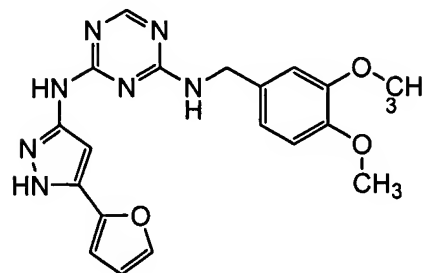
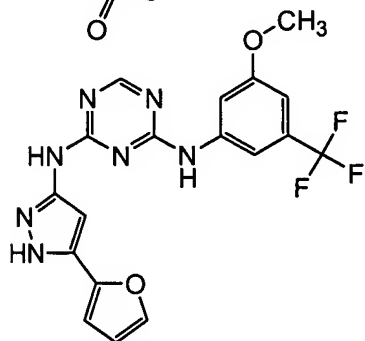
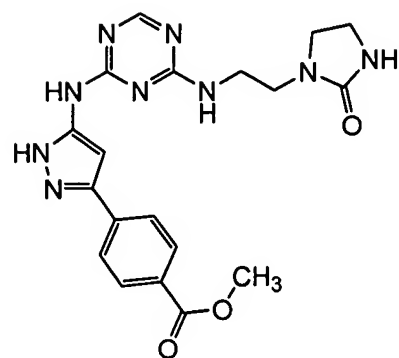
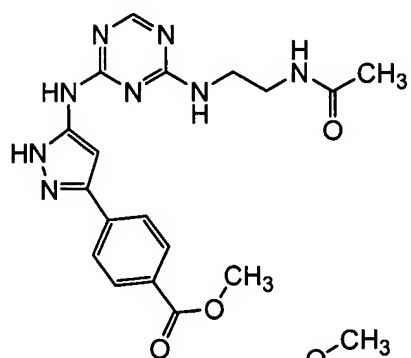
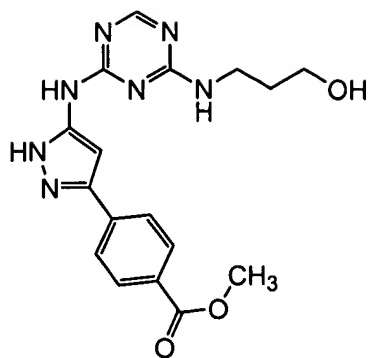
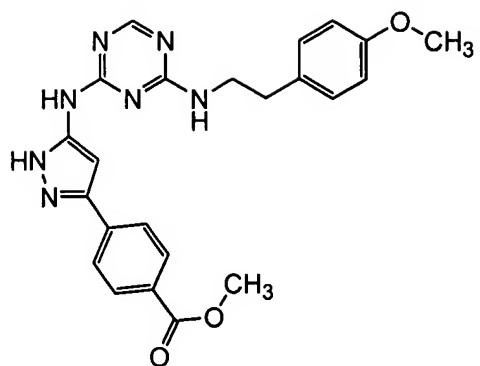


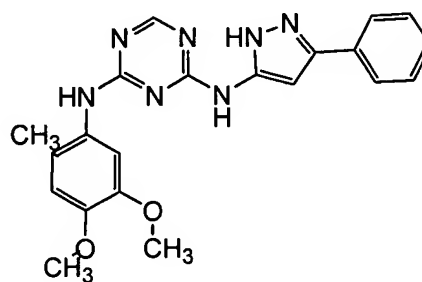
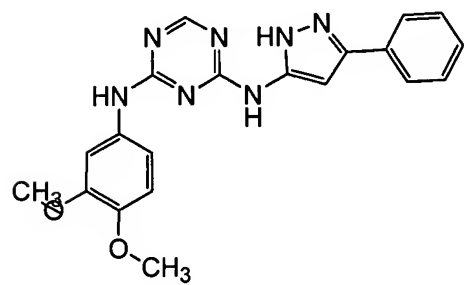
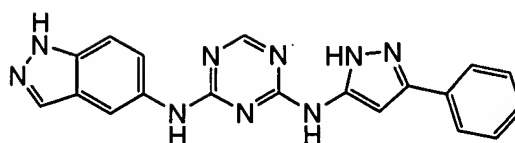
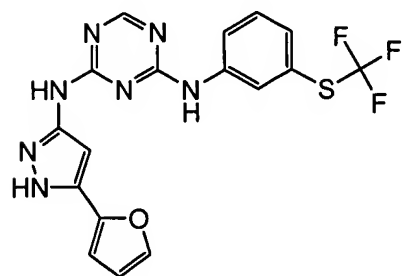
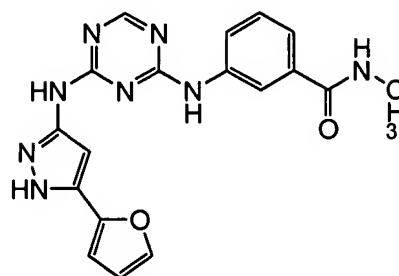
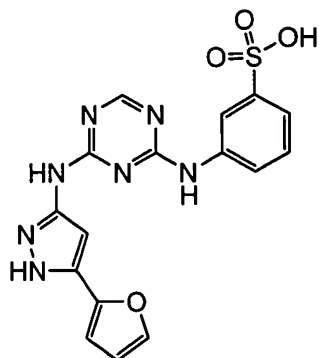
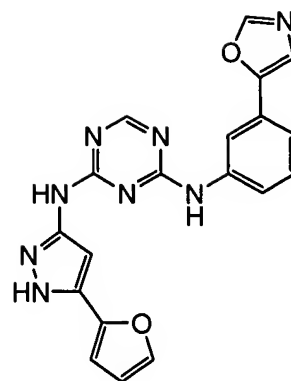
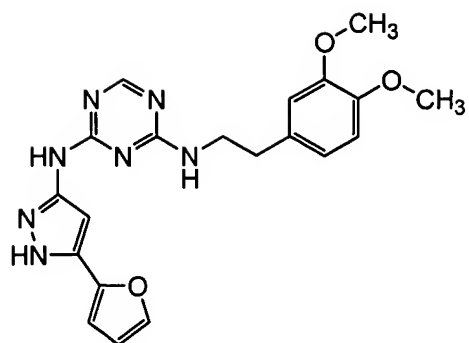


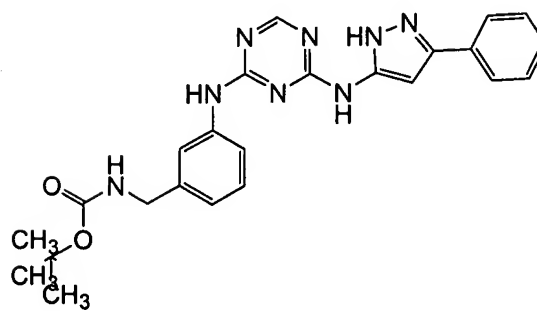
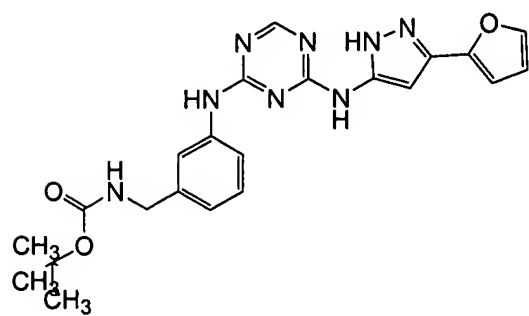
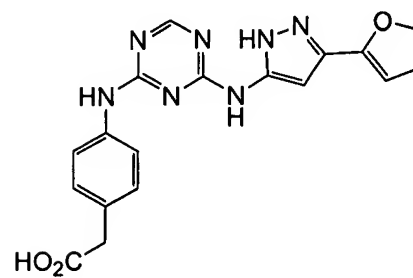
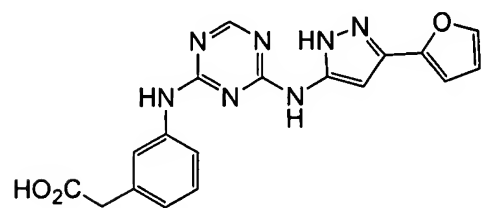
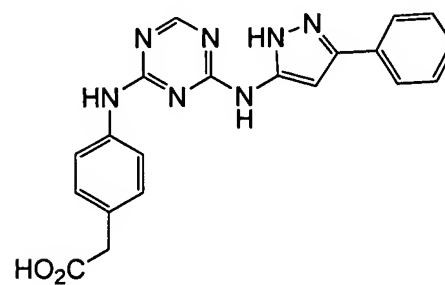
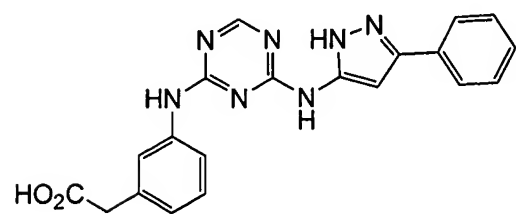
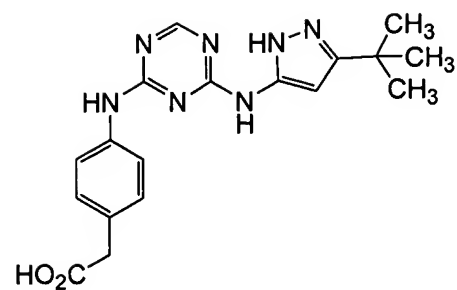
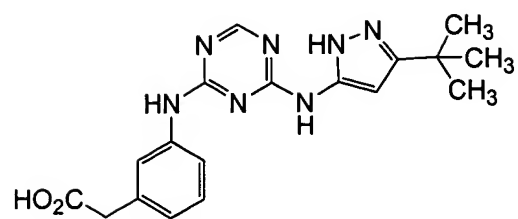


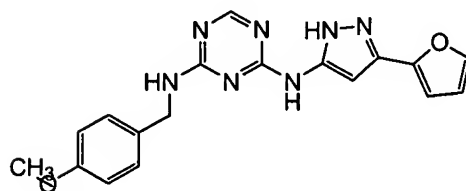
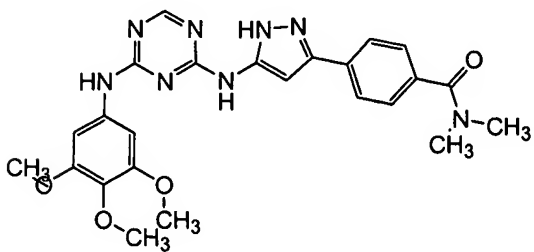
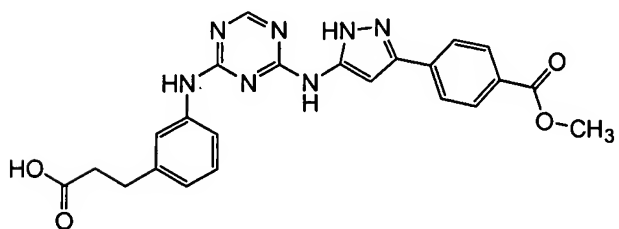
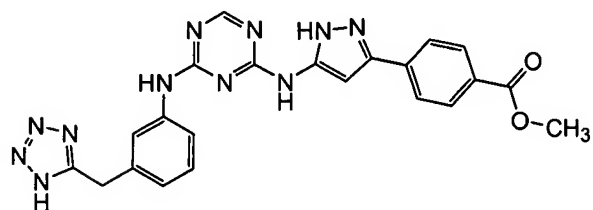
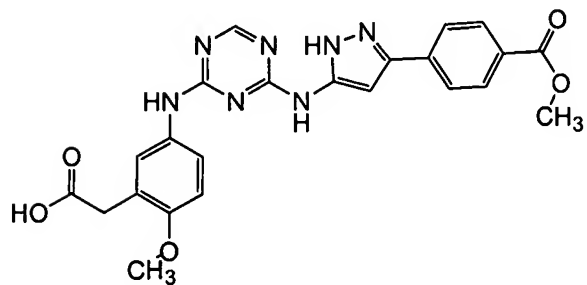
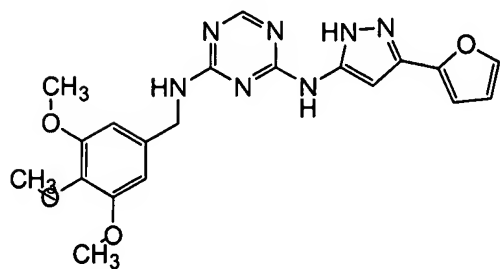
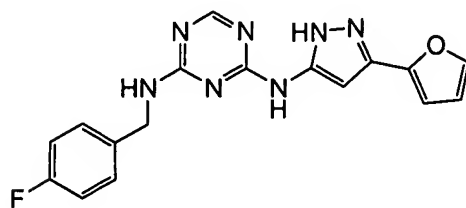
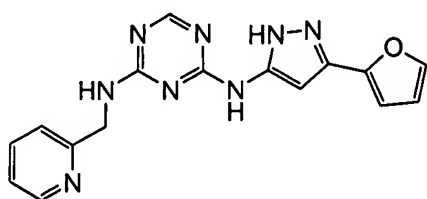
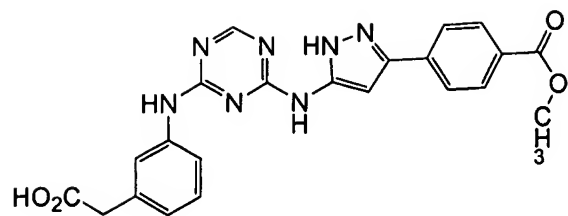
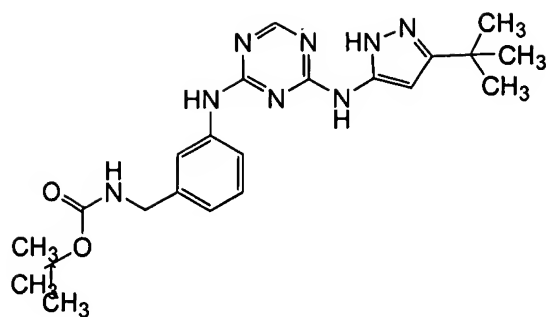


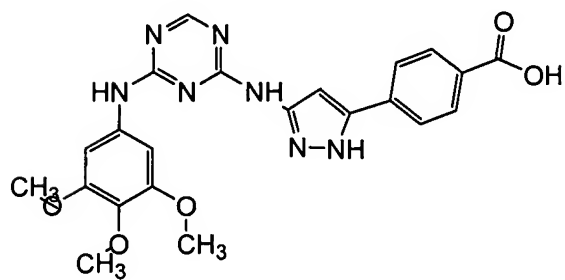
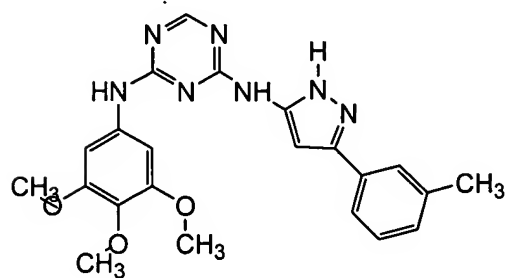
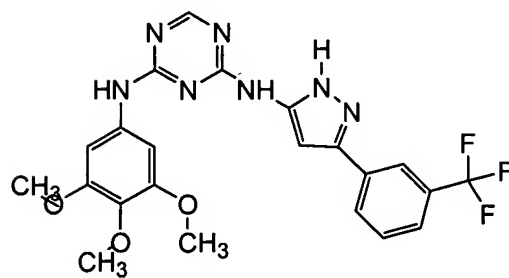
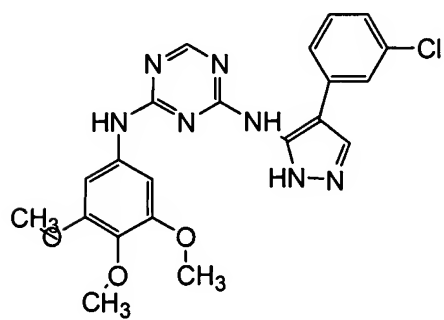
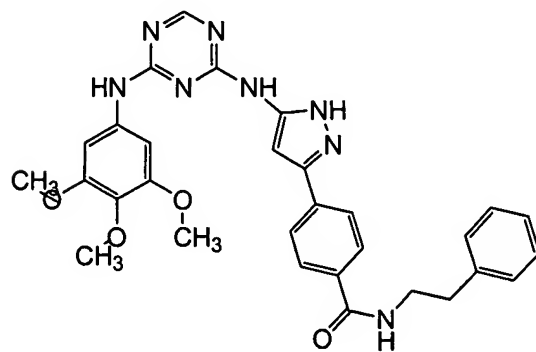
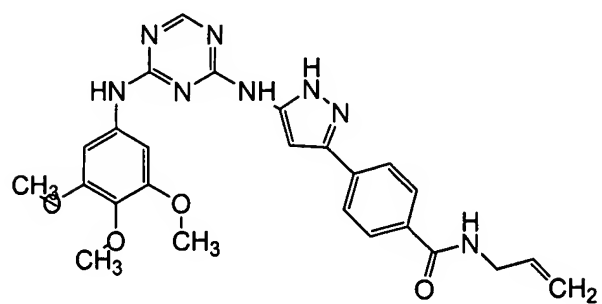
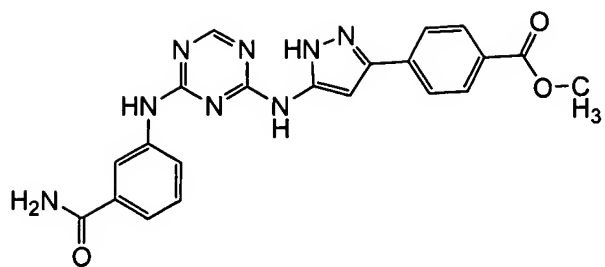
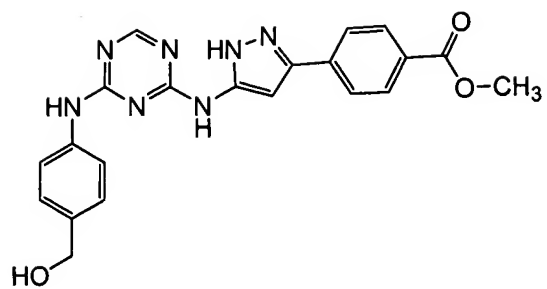


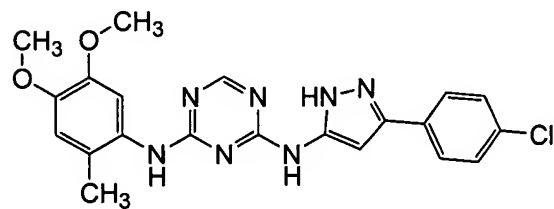
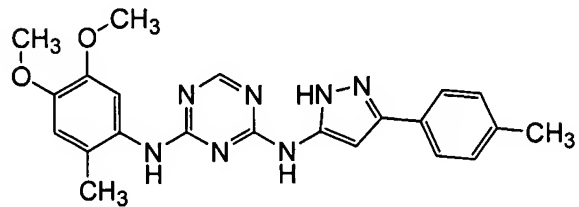
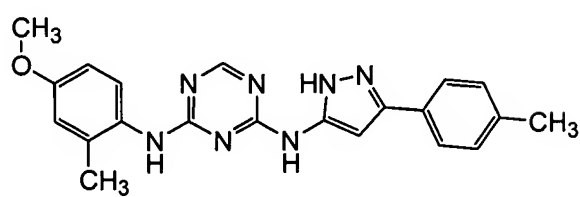
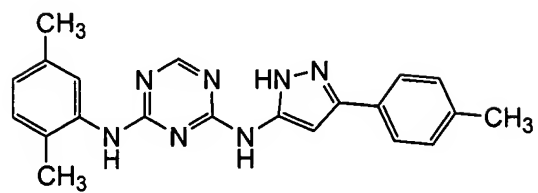
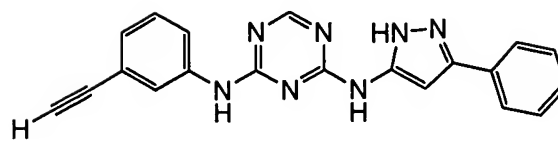
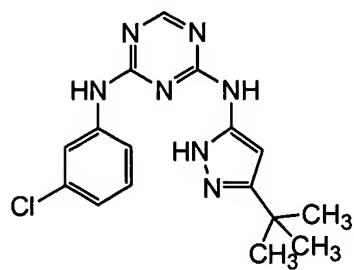
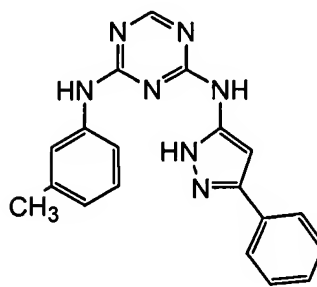
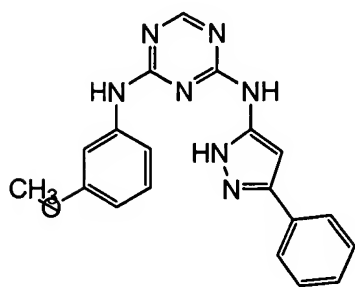
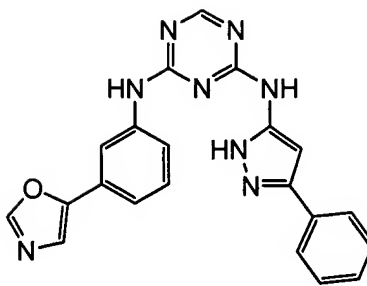
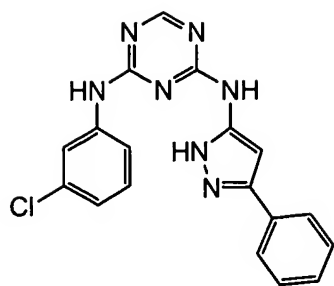


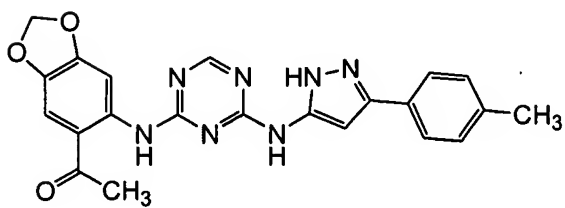
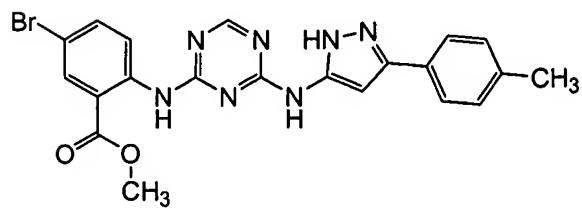
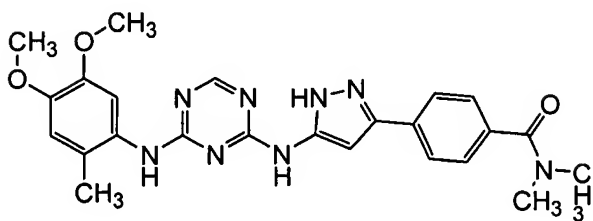
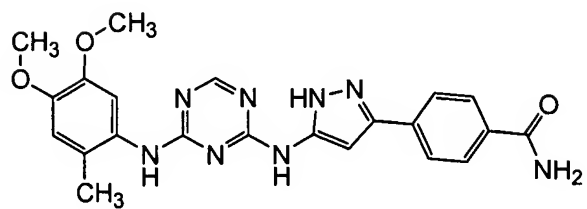
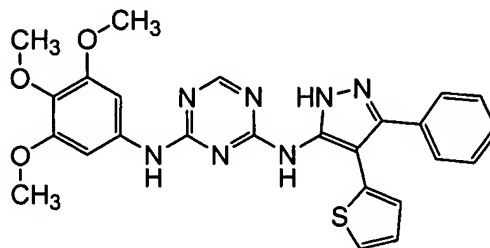
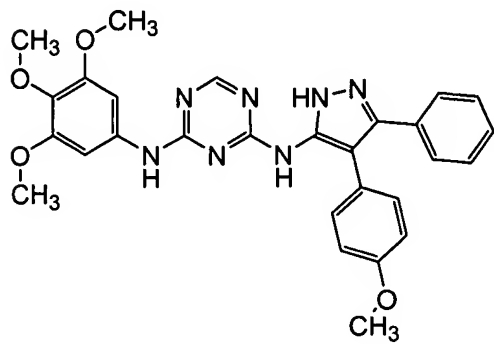
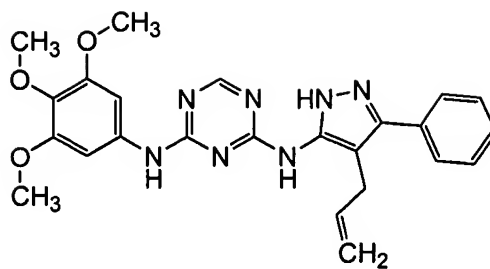
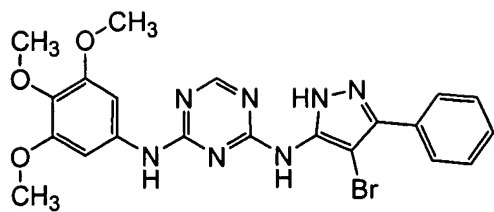


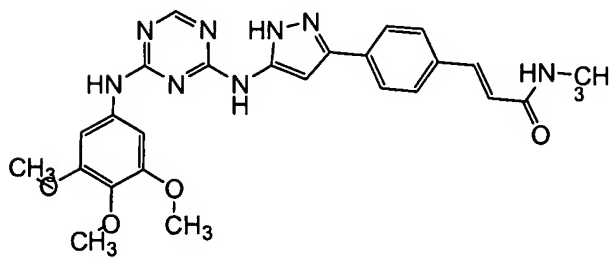
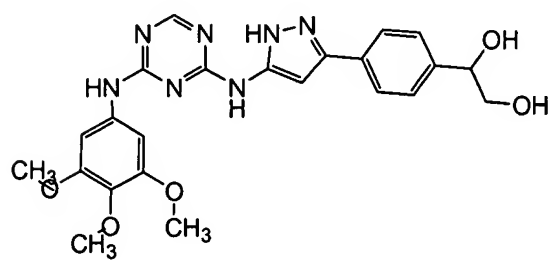
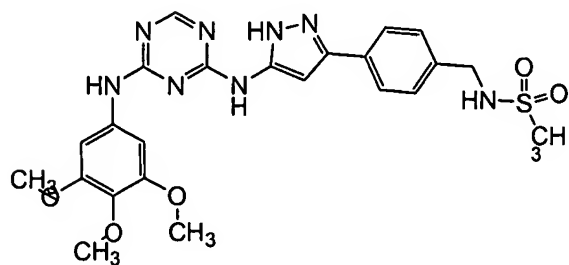
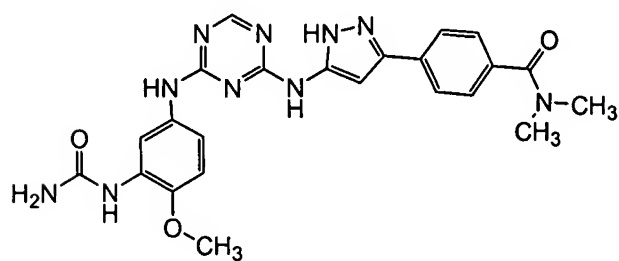
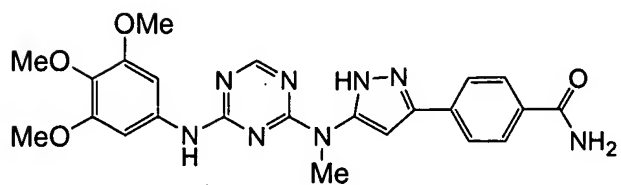
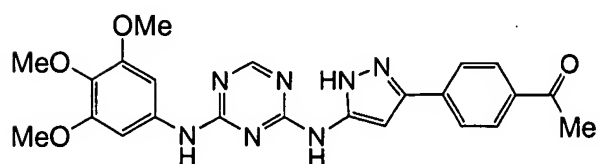
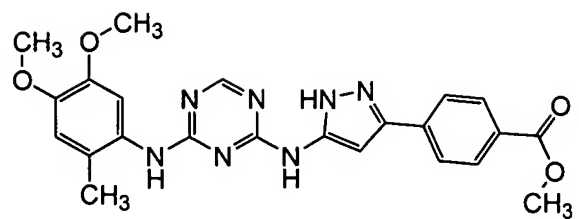
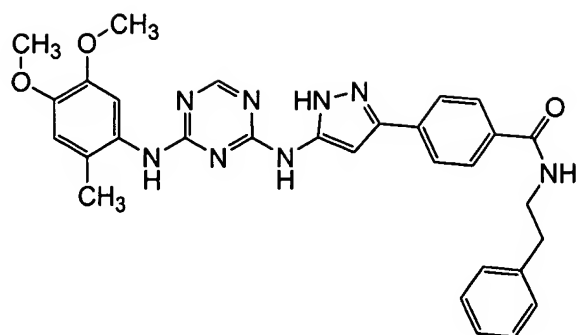


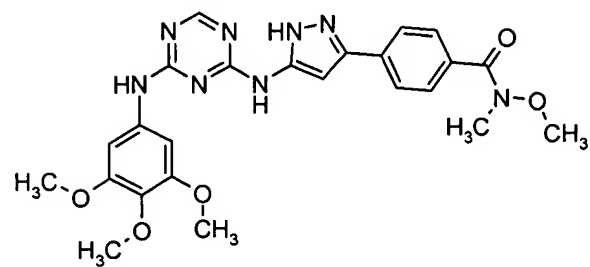
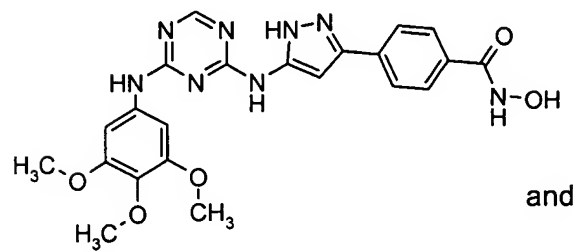
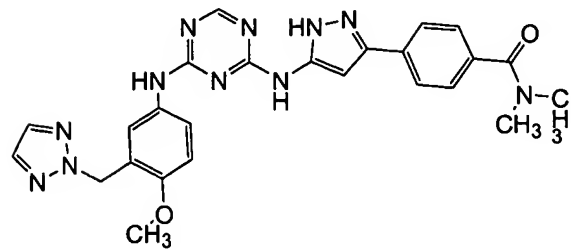
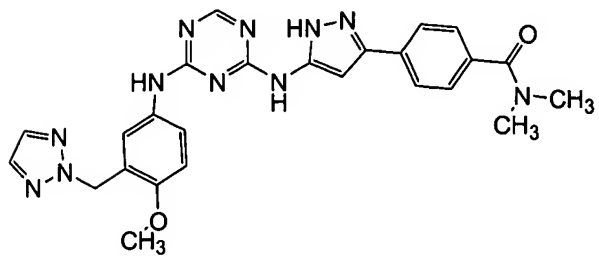
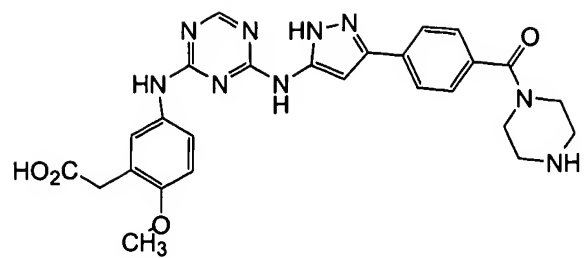












Claims 1, 6 and 22 were rejected under 35 USC §102(b) as being anticipated by Cutler et al. US 3,209,003. Applicants request reconsideration of the rejection in view of the amended Claims.

Claim 1 was rejected under 35 USC §102(b) as being anticipated by Fischer US 3,855,220. Applicants request reconsideration of the rejection in view of the amended Claims.

Claims 1, 6 and 22 were rejected under 35 USC §102(b) as being anticipated by Cutler et al. US 3,136,816. Applicants request reconsideration of the rejection in view of the amended Claims.

Claims 1, 6 and 22 were rejected under 35 USC §102(b) as being anticipated by Thurston US 2,474,194. Applicants request reconsideration of the rejection in view of the amended Claims.

Claims 1, 6, 8-9 and 30-31 were rejected under 35 USC §103(a) as being unpatentable over Newton et al. US 5,062,882. Newton describes tri-substituted triazines as herbicides (weed killers). There is no teaching as to the desirability of these compounds as pharmaceuticals, much less as kinase inhibitors. The pattern of preferences established by this reference also teaches away from the pyrazol-5-yl-amine substituted compounds of the current invention. The biological data described in Table 3 indicates that there was a substantial decrease in activity when R¹ is not methoxy (Examples 8-11). Therefore, assuming a medicinal chemist would look at herbicidal art, they would be taught away from the compounds of the present invention. Applicants contend that Newton et al. do not render obvious the pyrazol-5-yl-amine substituted triazines of the present invention.

Claims 1, 6 and 30-31 were rejected under 35 USC §103(a) as being unpatentable over Riebel et al. US 6,284,710 (the "'710" patent). Riebel et al. describe triazines as herbicides (weed killers). There is no teaching as to the desirability of these compounds as pharmaceuticals, much less as kinase inhibitors. In addition, the pre-emergent and post-emergent "spray and pray" test results provided in Tables A-B teach one skilled in agricultural chemistry away from the present invention. Examples 7, 11 and 52 were the only compounds that didn't kill every plant species (both crop and weed). This indicates that the "Z-substituent" was important for controlling non-